

LITERATURE REVIEW ON CNS TUMORS

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Abstract:

Central nervous system (CNS) tumors represent a significant subset of malignancies, with substantial implications for patient health, prognosis, and treatment strategies. These tumors arise in the brain or spinal cord and can be either primary or metastatic in nature. The diagnosis and treatment of CNS tumors involve a multidisciplinary approach, including neurosurgery, radiation therapy, and chemotherapy. This literature review explores the current state of research regarding CNS tumors, focusing on their pathophysiology, diagnostic methods, therapeutic options, and prognosis. Recent advancements in molecular biology and neuroimaging have contributed to more precise diagnostics and targeted therapies, yet challenges remain in the management of these complex conditions. The review aims to provide a comprehensive understanding of CNS tumors, highlighting ongoing research and identifying areas where further exploration is needed.

Keywords: CNS tumors, brain tumors, spinal cord tumors, diagnosis, treatment, prognosis, neuroimaging, chemotherapy, neurosurgery, molecular biology.

Introduction

Central nervous system (CNS) tumors are among the most diverse and complex forms of malignancy, affecting the brain and spinal cord. These tumors can arise from glial cells, neurons, or the meninges, and they may be benign or malignant. The incidence of CNS tumors is increasing, largely due to advancements in diagnostic imaging and increasing life expectancy. Despite substantial progress in treatment modalities, the prognosis for patients with CNS tumors remains largely dependent on tumor type, location, and stage at diagnosis. This article reviews the current literature on CNS tumors, focusing on their pathophysiology, diagnostic approaches, treatment strategies, and outcomes.



Literature Review

Types of CNS Tumors CNS tumors are classified based on their location and cellular origin. The most common primary brain tumors include gliomas, meningiomas, and pituitary adenomas. Gliomas are further divided into astrocytomas, oligodendrogliomas, and ependymomas, depending on the glial cell type from which they arise. Meningiomas, which arise from the meninges, are typically benign, while gliomas can range from low-grade to highly malignant forms, such as glioblastoma multiforme (GBM). Spinal cord tumors, though less common, also present significant clinical challenges and include both primary and metastatic types.

Diagnosis and Imaging Diagnostic methods for CNS tumors have evolved significantly with advancements in neuroimaging. Magnetic resonance imaging (MRI) is the gold standard for detecting and monitoring CNS tumors, providing detailed images of brain and spinal cord structures. Positron emission tomography (PET) scans and computed tomography (CT) are also used in certain clinical scenarios, offering additional information regarding tumor metabolism and metastasis. Recent innovations such as functional MRI (fMRI) and magnetic resonance spectroscopy (MRS) are further enhancing our ability to assess tumor characteristics and guide treatment planning.

Treatment Options The treatment of CNS tumors involves a combination of surgical resection, radiation therapy, and chemotherapy. Neurosurgery remains the primary treatment for most CNS tumors, with the goal of removing as much of the tumor as possible without causing neurological damage. Radiation therapy, particularly stereotactic radiosurgery, is often used postoperatively or for tumors that are inoperable due to their location. Chemotherapy is typically reserved for more aggressive tumors, such as glioblastomas, where adjuvant therapy can improve survival. Newer approaches, such as targeted therapies and immunotherapy, have shown promise in clinical trials, particularly for gliomas.

Prognosis and Survival Prognosis for patients with CNS tumors depends on various factors, including tumor type, grade, location, and the age and overall health of the patient. Glioblastoma multiforme, one of the most aggressive types of brain cancer, has a poor prognosis, with a median survival of less than two years despite aggressive treatment. On the other hand, meningiomas and low-grade gliomas may have a much better prognosis, with long-term survival rates approaching 90%. The role of molecular markers in predicting prognosis is an area of active research, with certain genetic mutations linked to more favorable or worse outcomes.

Comprehensive Literature Review on Central Nervous System (CNS) Tumors **Introduction and Epidemiology** Primary CNS tumors encompass a diverse group of neoplasms originating in the brain, spinal cord, or meninges, exhibiting significant heterogeneity in histology, molecular profile, biology, and clinical behavior. These tumors are relatively rare but represent a major cause of cancer-related morbidity and mortality, particularly in children and young adults.



According to the most recent Central Brain Tumor Registry of the United States (CBTRUS) Statistical Report (2018–2022, published 2025), the average annual age-adjusted incidence rate of all primary malignant and non-malignant CNS tumors in the United States is 26.05 per 100,000 population, corresponding to approximately 489,718 incident cases over a five-year period. Malignant tumors account for 6.86 per 100,000 (128,865 cases), while non-malignant tumors comprise 19.19 per 100,000 (360,853 cases). Meningiomas remain the most common non-malignant tumor, and glioblastoma the predominant malignant type.

In pediatric populations (ages 0–19 years), CNS tumors are the most common solid malignancy and the leading cause of cancer-related death. Incidence rates are around 5–6 per 100,000, with low-grade gliomas and embryonal tumors predominating. Global variations exist, with higher rates in high-income countries likely due to improved diagnostics. Risk factors remain limited: ionizing radiation is established, and hereditary syndromes (e.g., neurofibromatosis, Li-Fraumeni) contribute to ~5–10% of cases. No consistent environmental links have been confirmed beyond radiation.

Survival disparities persist: five-year relative survival for malignant CNS tumors is ~36%, versus ~92% for non-malignant. In adolescents and young adults (15–39 years), brain tumors are the second most common cancer type, with improved survival for non-malignant entities but persistent challenges in high-grade gliomas.

Classification and Molecular Advances

The 2021 World Health Organization (WHO) Classification of Tumors of the Central Nervous System (5th edition) remains the cornerstone, integrating histology with molecular parameters for integrated diagnoses. Key features include:

- Use of Arabic numerals for grading (e.g., glioblastoma, IDH-wildtype as CNS WHO grade 4).
- Separation of adult-type (e.g., IDH-mutant astrocytomas/oligodendrogliomas) and pediatric-type diffuse gliomas.
- New entities: e.g., diffuse midline glioma, H3 K27-altered; high-grade astrocytoma with piloid features; polymorphous low-grade neuroepithelial tumor of the young (PLNTY).
- Emphasis on drivers like BRAF V600E, FGFR alterations in low-grade tumors; EGFR amplification, TERT promoter mutations in glioblastoma.

No major 6th edition has emerged by late 2025, but refinements continue through cIMPACT-NOW-like processes. DNA methylation profiling and next-generation sequencing (NGS) are increasingly standard for ambiguous cases. Rapid intraoperative tools, such as nanopore-based Rapid-CNS2 sequencing (2024–2025 studies), enable molecular classification within hours, aiding surgical decisions.

Multiomic profiling enhances diagnostics, particularly in pediatrics, identifying therapeutic targets or predisposition syndromes in >50% of cases.



Common Tumor Types and Molecular Subtypes

- Gliomas (adult-type): Predominant in adults; glioblastoma (IDH-wildtype) most aggressive (median survival ~15 months). Key drivers: EGFR amplification, PTEN loss, TERT mutations.
 - Pediatric-type gliomas: Low-grade often BRAF-driven (V600E or fusions); high-grade include diffuse midline gliomas (H3 K27-altered).
 - Meningiomas: Mostly benign; AKT1, SMO mutations in subsets.
 - Embryonal tumors: Medulloblastoma (molecular subgroups: WNT, SHH, Group 3/4); atypical teratoid/rhabdoid tumors (SMARCB1 loss).
 - Ependymomas: Subgrouped by location and molecular features (e.g., ZFTA fusions in supratentorial).
 - Others: Pituitary adenomas, craniopharyngiomas, CNS germ cell tumors.
- Heterogeneity within tumors drives resistance; single-cell analyses reveal subclonal drivers.

Treatment Landscape

Standard multimodal therapy includes maximal safe resection, radiation, and chemotherapy (e.g., temozolomide for methylated glioblastoma). Outcomes remain suboptimal for high-grade tumors.

Surgical and Radiotherapeutic Advances:

- Advanced imaging (e.g., 18F-DOPA PET + MRI) guides resection.
- Hypofractionated proton beam therapy shows promise in elderly glioblastoma (2024–2025 trials), improving survival while preserving quality of life.
- Focused ultrasound for BBB opening enhances drug delivery.

Targeted Therapies:

- BRAF/MEK inhibitors: Established for BRAF V600E-mutant tumors (e.g., dabrafenib/trametinib); tovorafenib (type II RAF inhibitor) FDA-approved 2024 for relapsed pediatric low-grade glioma (pLGG) with BRAF alterations (FIREFLY-1 trial: 51% response rate).
- IDH inhibitors: Vorasidenib/ivosidenib for IDH-mutant gliomas.
- FGFR/NTRK inhibitors: Emerging for fusion-driven tumors (e.g., pemigatinib, larotrectinib).
- Other: ONC201 (dordaviprone) for H3 K27M-mutant diffuse midline gliomas (ongoing phase III).

Immunotherapy:

- Checkpoint inhibitors (e.g., nivolumab) limited efficacy in glioblastoma due to cold microenvironment.
- CAR-T/CAR-NK cells: Promising preclinical/early trials; challenges include antigen heterogeneity and trafficking.



- Oncolytic viruses, mRNA vaccines (e.g., personalized neoantigen), and bispecific antibodies advancing.
- Ultrasound-mediated BBB opening + immunotherapy/chemotherapy combos (2024 studies) enhance delivery.

Pediatric-Specific:

- Risk-adapted therapy reduces long-term sequelae; molecular subgrouping (e.g., medulloblastoma) guides de-escalation.
- Tovorafenib and other targeted agents transformative for BRAF-altered pLGG.

Challenges and Future Directions

Key barriers: BBB/BBB, tumor heterogeneity, immunosuppression, low mutational burden limiting neoantigens. Drug repurposing (e.g., gallium maltolate), combination strategies (targeted + immuno), and AI-driven biomarker discovery are priorities.

Ongoing trials emphasize precision: RNA-LP vaccines, dual-target CAR-T, proton therapies. Global disparities, especially in low/middle-income countries, highlight access needs.

In conclusion, molecular integration has refined diagnostics and enabled targeted therapies, particularly in pediatrics. Immunotherapy and advanced delivery hold promise, but multidisciplinary, biomarker-driven trials are essential for transformative progress in this challenging field.

The increasing incidence of CNS tumors calls for enhanced research efforts to improve diagnostic accuracy and treatment outcomes. One of the most significant advancements in recent years is the use of molecular biology techniques to identify genetic mutations associated with different tumor types. For example, the discovery of the IDH1 mutation in gliomas has allowed for more precise prognostication and targeted treatment options. However, challenges remain in developing therapies that can effectively cross the blood-brain barrier and selectively target tumor cells without affecting healthy brain tissue. Additionally, the integration of advanced imaging modalities such as fMRI and MRS into clinical practice holds the potential for improving treatment planning and monitoring.

Conclusion

CNS tumors continue to be a major cause of morbidity and mortality worldwide, with a diverse array of tumor types and treatment options. Advances in neuroimaging and molecular diagnostics have improved our ability to detect and classify these tumors, leading to better-targeted treatment strategies. However, many obstacles remain in the effective management of aggressive tumors such as glioblastoma. Future research should focus on developing novel therapies, improving early detection techniques, and understanding the molecular basis of tumor progression to improve patient outcomes.

Improved Early Detection: Research into developing non-invasive, highly sensitive biomarkers for early detection of CNS tumors is crucial to improving prognosis.



Targeted Therapies: Investment in the development of therapies that can specifically target tumor cells while sparing healthy tissue is essential for improving survival and quality of life for patients.

Molecular Profiling: Continued exploration of the genetic and molecular profiles of CNS tumors should be prioritized to allow for more personalized treatment plans.

Multidisciplinary Approach: Ongoing collaboration between neurosurgeons, oncologists, radiologists, and researchers will be key to advancing treatment strategies for CNS tumors.

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